

- Q1*
1. (Amended) A polyclonal antisera composition of a transgenic nonhuman animal which generates antibody diversity predominately by gene conversion, wherein said antisera composition specifically recognizes an immunogen and comprises immunoglobulin protein molecules comprised of at least a portion of a human immunoglobulin polypeptide sequence, and wherein said immunoglobulin protein molecules specifically bind to said immunogen.
  2. (Amended) The polyclonal antisera according to Claim 1, wherein said portion of the human immunoglobulin polypeptide sequence is a portion of a human immunoglobulin heavy chain polypeptide sequence.
  4. (Amended) The polyclonal antisera composition according to Claim 1 or 33, wherein said transgenic nonhuman animal is from the order *Lagomorpha*.
  5. (Amended) The polyclonal antisera composition according to Claim 2, wherein said portion of the human heavy chain polypeptide sequence comprises a polypeptide sequence encoded by a human heavy chain constant region element.

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  6. (Amended) The polyclonal antisera composition according to Claim 5, wherein said portion of the human heavy chain polypeptide sequence further comprises a polypeptide sequence encoded by a human heavy chain variable region element.
  7. (Amended) The polyclonal antisera composition according to Claim 6, wherein said human variable region element has replaced the endogenous variable region element proximal to the D region.
  8. (Amended) The polyclonal antisera composition according to Claim 1, wherein said immunogen comprises a disease causing organism or antigenic portion of said organism.

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11. (Amended) A transgenic nonhuman animal which generates antibody diversity predominately by gene conversion, comprising at least a portion of functional human heavy chain immunoglobulin genes integrated by homologous recombination into the genome of said animal, wherein said portion of the functional human heavy chain immunoglobulin genes rearranges in frame with immunoglobulin heavy chain sequences endogenous to said nonhuman animal to encode functional antibody molecules that comprise at least a portion of a human immunoglobulin heavy chain polypeptide sequence, and wherein said animal produces said functional antibody molecules when immunized.

12. (Amended) A transgenic nonhuman animal which generates antibody diversity predominately by gene conversion, comprising at least a portion of functional human immunoglobulin light chain genes integrated by homologous recombination into the genome of said animal, wherein said portion of the human immunoglobulin light chain genes rearranges in frame with immunoglobulin light chain sequences endogenous to said nonhuman animal to encode functional antibody molecules that comprise at least a portion of a human immunoglobulin light chain polypeptide sequence, and wherein said animal produces said functional antibody molecules when immunized.

14. (Amended) The transgenic nonhuman animal according to Claim 11 or 12, wherein said transgenic nonhuman animal is from the order *Lagomorpha*.

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15. (Amended) The transgenic nonhuman animal according to Claim 11, wherein said portion of the functional human immunoglobulin heavy chain genes comprises at least one human heavy chain constant region element.

16. (Amended) The transgenic nonhuman animal according to Claim 15, wherein said portion of the functional human immunoglobulin heavy chain genes further comprises at least one human heavy chain variable region element.

17. (Amended) The transgenic nonhuman animal according to Claim 16, wherein said human variable region element has replaced the endogenous variable region element proximal to the D region.

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18. (Amended) The transgenic nonhuman animal according to Claim 12, wherein said portion of the human immunoglobulin light chain genes encodes the κ chain.

19. (Amended) An antisera composition produced by the transgenic nonhuman animal according to any one of claims 11-18.

26. (Amended) A method of producing a transgenic nonhuman animal which generates antibody diversity predominately by gene conversion, comprising at least a portion of human immunoglobulin genes integrated into the genome of the non-human animal, wherein said transgenic nonhuman animal produces functional antibody molecules comprised of at least a portion of a human immunoglobulin polypeptide sequence when immunized, said method comprising:

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producing a first mutated animal neonate which comprises immunoglobulin heavy chain loci wherein at least one of a constant region element or a variable region element endogenous to the non-human animal is replaced with a human heavy chain constant region element or a human heavy chain variable region element, by genetically altering a cell nucleus of the non-human animal, introducing the genetically altered cell nucleus into a first enucleated nuclear transfer unit cell, and introducing the first nuclear transfer unit cell which comprises the genetically altered nucleus into a female recipient host to produce said first mutated neonate;

producing a second mutated animal neonate which comprises immunoglobulin light chain loci wherein at least one of a constant region element or a variable region element endogenous to the non-human animal is replaced with a human light chain constant region element or a human light chain variable region element, by genetically altering a cell nucleus of the non-human animal, introducing the genetically altered cell nucleus into a second enucleated nuclear transfer unit cell, introducing the second nuclear

transfer unit cell which comprises the genetically altered nucleus into a female recipient host to produce a second mutated neonate; breeding mature first and second mutated neonates and selecting a transgenic non-human animal which produces functional antibody molecules comprised of at least a portion of a human immunoglobulin polypeptide sequence when immunized.

27. (Amended) A method of producing a transgenic nonhuman animal which generates antibody diversity predominately by gene conversion, comprising at least a portion of human immunoglobulin genes integrated into the genome of the non-human animal, wherein said transgenic non-human animal produces functional antibody molecules comprised of at least a portion of a human immunoglobulin heavy chain polypeptide sequence and at least a portion of a human immunoglobulin light chain polypeptide sequence when immunized, said method comprising:

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producing a mutated animal neonate which comprises immunoglobulin heavy and light chain loci wherein at least one of a heavy chain constant region element or a heavy chain variable region element endogenous to the non-human animal is replaced with a human heavy chain constant region element or a human heavy chain variable region element, and wherein at least one of a light chain constant region element or a light chain variable region element endogenous to the non-human animal is replaced with a human light chain constant region element or a human light chain variable region element, by genetically altering a cell nucleus of the non-human animal, introducing the genetically altered cell nucleus into an enucleated nuclear transfer unit cell, and introducing the nuclear transfer unit cell which comprises the genetically altered cell nucleus into a female recipient host to produce said mutated neonate; growing said mutated neonate, and determining said neonate as capable of producing antibody molecules comprised of at least a portion of a human immunoglobulin heavy chain polypeptide sequence and at least a portion of a human immunoglobulin light chain polypeptide sequence thereby producing said transgenic non-human animal.

30. (Amended) A method according to Claim 26, wherein said first mutated neonate comprises a heavy chain locus wherein at least one constant region element endogenous to the non-human animal is replaced with a human heavy chain constant region element.

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31. (Amended) A method according to Claim 26, wherein said first mutated neonate comprises a heavy chain locus wherein at least one variable region element endogenous to the non-human animal is replaced with a human heavy chain variable region element.

32. (Amended) A method according to Claim 31, wherein said variable region element endogenous to the non-human animal is the variable region element proximal to the D region.

**Please add the following claims:**

33. The polyclonal antisera according to Claim 1, wherein said portion of the human immunoglobulin polypeptide sequence is a portion of a human immunoglobulin light chain polypeptide sequence.

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34. The polyclonal antisera composition according to Claim 33, wherein said portion of the human light chain polypeptide sequence comprises a polypeptide sequence encoded by a human light chain constant region element.

35. The polyclonal antisera composition according to Claim 33, wherein said portion of the human light chain polypeptide sequence further comprises a polypeptide sequence encoded by a human light chain variable region element.

36. A polyclonal antisera composition of a transgenic non-human animal which generates antibody diversity predominately by gene conversion, comprising immunoglobulin protein molecules comprised of at least a portion of a human immunoglobulin polypeptide sequence and at least a portion of an immunoglobulin polypeptide sequence

endogenous to the animal, wherein said immunoglobulin protein molecules specifically recognize an immunogen.

37. The polyclonal antisera composition according to Claim 36, wherein said portion of the human immunoglobulin polypeptide sequence is a portion of a human heavy chain polypeptide sequence.
38. The polyclonal antisera composition according to Claim 37, wherein said portion of the human heavy chain polypeptide sequence comprises a polypeptide sequence encoded by a human heavy chain constant region element.
39. The polyclonal antisera composition according to Claim 38, wherein said portion of the human heavy chain polypeptide sequence further comprises a polypeptide sequence encoded by a human heavy chain variable region element.
- Q 7
40. The polyclonal antisera composition according to Claim 36, wherein said portion of the human immunoglobulin polypeptide sequence is a portion of a human light chain polypeptide sequence.
41. The polyclonal antisera composition according to Claim 40, wherein said portion of the human light chain polypeptide sequence comprises a polypeptide sequence encoded by a human light chain constant region element.
42. The polyclonal antisera composition according to Claim 41, wherein said portion of the human light chain polypeptide sequence further comprises a polypeptide sequence encoded by a human light chain variable region element.
43. A method of producing a transgenic non-human animal comprising at least a portion of human immunoglobulin genes integrated into the genome of the animal, wherein said transgenic non-human animal generates antibody diversity predominately by gene conversion and produces functional antibody molecules comprised of at least a portion of

a human immunoglobulin heavy chain polypeptide sequence when immunized, said method comprising:

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producing a mutated animal neonate which comprises immunoglobulin heavy chain loci wherein at least one of a heavy chain constant region element or a heavy chain variable region element endogenous to the animal is replaced with a human heavy chain constant region element or a human heavy chain variable region element, by genetically altering a cell nucleus of the animal, introducing the genetically altered cell nucleus into an enucleated nuclear transfer unit cell, and introducing the nuclear transfer unit cell which comprises the genetically altered cell nucleus into a female recipient host to produce said mutated neonate;

growing said mutated neonate and determining the neonate as capable of producing antibody molecules comprised of at least a portion of a human immunoglobulin heavy chain polypeptide sequence thereby producing said transgenic non-human animal.

44. A method of producing a transgenic non-human animal comprising at least a portion of human immunoglobulin genes integrated into the genome of said rabbit, wherein said transgenic non-human animal generates antibody diversity predominately by gene conversion and produces functional antibody molecules comprised of at least a portion of a human immunoglobulin light chain polypeptide sequence when immunized, said method comprising:

producing a mutated animal neonate which comprises immunoglobulin light chain loci wherein at least one of a light chain constant region element or a light chain variable region element endogenous to the animal is replaced with a human light chain constant region element or a human light chain variable region element, by genetically altering a cell nucleus of the animal, introducing the genetically altered cell nucleus into an enucleated nuclear transfer unit cell, and introducing the nuclear transfer unit cell which comprises the genetically altered cell nucleus into a female recipient host to produce said mutated neonate;

growing said mutated neonate and determining the neonate as capable of producing antibody molecules comprised of at least a portion of a human